REMARKS

I. Status

Claims 1-15 are pending in the application. Claims 3, 8, 10, and 14-15 are withdrawn. Claim 1 is currently amended with regard to variable Z. Claim 11 is currently amended to be in independent form. Claim 12 is currently amended to correct certain errors of a typographical nature, which were originally presented unintentionally and in good faith. No new matter is being added by the currently amendments.

Claims 12-13 stand rejected under 35 U.S.C. § 112, ¶1 with regard to the enablement and written description requirements. Claim 1 stands rejected under 35 U.S.C. § 112, ¶2. Claims 1-2, 4-9, and 12-13 stand rejected under 35 U.S.C. § 102(g) over US 2004/0157886 ("Domany").

At the outset, Applicants thank the Examiner for the indication that claim 11 is merely objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. Claim 11 is currently amended in accordance with the Examiner's suggestion. As such, claim 11 is in condition for allowance.

II. Claims 12 and 13 Are Enabled and Satisfy the Written Description Requirement

Claims 12-13 stand rejected under § 112, ¶1 with regard to the enablement and written description requirements. Applicants traverse each of the rejections, which are discussed separately below.

Enablement:

Claim 12 defines a pharmaceutical composition for treating or preventing certain disorders or conditions, wherein the composition comprises an amount of a compound according to claim 1,

or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorders or conditions and a pharmaceutically acceptable carrier. Claim 13 defines a pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by inhibiting MIP-1α and/or RANTES binding to the receptor CCR1 in a mammal, comprising an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, effective in treating or preventing such disorders or conditions and a pharmaceutically acceptable carrier.

The Examiner asserts that the claims contain subject matter that is supposedly not described in the specification to enable one of skill in the art to make and/or use the invention. The Examiner then attempts to support this assertion by citing the *In re Wands* factors at page 3 of the Office Action: (i) the nature of the invention; (ii) the state of the art and predictability; (iii) the amount of guidance and working examples.

With regard to the nature of the invention, the Examiner merely states, "The claims are drawn to pharmaceutical composition[s] of the claimed compounds for 'treating or preventing a disorder or condition. . .that can be treated or prevented by inhibiting MIP-1α and/or RANTES binding to the receptor CCR1.'" This statement, however, does not help establish that the specification does not enable the subject matter defined by claims 12 and 13, and the Examiner has not indicated with specificity how this factor helps establish that point, which it does not. As the Examiner knows, a proper assessment of *In re Wands* factors begins with assessing the nature of the invention, which becomes the backdrop to determine the state of the art and the level of skill in the art. MPEP § 2164.05(a) (8th ed. 2001, rev. 2004).

The state of the art, which is the second factor cited by the Examiner, refers to what one of

ordinary skill in the art would have known at the time the application was filed about the subject matter to which the claimed invention pertains. *Id.* Concerning this factor, the Examiner asserts with generality that cytokine receptor function has been known to be highly unpredictable and a specific nexus from a specific cytokine cannot be extrapolated to the therapeutic effects claimed. Applicants contend, however, that the state of the art at the time the application was filed was such that those of skill in the art would have known of a nexus between the CCR1 receptor and the cited immune based diseases. The present application was filed provisionally on July 18, 2002. At that time, those of skill in the art would have benefited from certain publications disclosing pharmaceutical compositions comprising certain piperazine compounds for treating or preventing a disorder or condition that can be treated or prevented by inhibiting MIP-1α and/or RANTES binding to the receptor CCR1, e.g., WO 01/72728 entitled "Novel Piperazine Derivatives" published October 4, 2001 and WO 02/32901 entitled "Bridged Piperazine Derivatives" published April 25, 2002. Besides the cited publications, the present disclosure provides additional support, e.g., at pages 1-2 and citations therein, for there being a nexus between the cited diseases and the CCR1 receptor. At least in view of the evidence cited, the state of the art at the time the application was filed supported a nexus between the cited diseases and the CCR1 receptor and accordingly increased the predictability in the art.

Lastly, with regard to the amount of guidance and working examples, the Examiner asserts that there is supposedly no disclosure on what effect on the receptor binding with any of the disclosed compounds. Indeed, the specification discloses at page 39, line 13 that all of the exemplified compounds had an IC_{50} value of less than 10μM in the Chemotaxis assay. Certainly, in view of the nine examples and the subgenuses disclosed in the application, e.g., in the dependent

compound claims, those of skill in the art have ample guidance "as to how to pick and choose compounds for dosage formulation." Further, the Examiner appears to believe that the "effective" amount of claims 12-13 is not enabling, however, Applicants disclose in the specification, e.g., at page 40, line 28-32, proposed dosages. In addition, the present disclosure teaches those of skill in the art how to make and use the claimed compositions, e.g., at p. 39, line 15 - page 41, line 24. Because of the ample guidance in the specification, those of skill in the art would be able to make and use the compositions defined by claims 12-13.

Therefore, in view of the *In re Wands* factors cited by the Examiner, it is apparent that those of skill in the art would be enabled to make and use the compositions defined by claims 12-13. Even so, the Examiner does not discuss all of the *In re Wands* factors, presumably because the other factors do not support that the Examiner's position that the specification does not enable the compositions defined by claims 12-13. In all, there are eight *In re Wands* factors. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Indeed, when one considers the other following factors, it becomes even more apparent that claims 12-13 are properly enabled:

- Quantity of Experimentation Necessary: The Federal Circuit has made it clear that enablement only requires that the specification teach those in the art to make and use the invention *without undue experimentation.* (Emphasis added). *Id.* citing *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986), cert. denied, 480 U.S. 947. "The key word is 'undue,' not 'experimentation.'" *Id.* citing *In re Angstadt*, 537 F.2d at 498, 504 (C.C.P.A. 1976). As discussed above, the specification provides ample guidance at least by virtue of the examples and subgenus claims that enable those of skill in the art to make and use the claimed compositions. Arriving at the claimed compositions requires mere routine experimentation, which is permissible.

Id. citing *In re Jackson*, 217 USPQ 804, 807 (Bd. Pat. App. & Int. 1982). Indeed, those of skill in the art are prepared to do such experimentation similar to practitioners of the biotechnical art. *Id.* at 740. As such, the quantity of experimentation required by those of skill in the art to arrive at the claimed compositions is neither unreasonable nor undue.

- Breadth of the Claims: The breadth of the claims is appropriate in view of the nexus between the CCR1 receptor and the cited immune based diseases, as discussed above.
- The Relative Level of Skill of Those in the Art: It is certain that the level of skill in the art pertinent here is high. When overturning the lower decision of the BPAI, the Court of Appeals for the Federal Circuit believed a high level of skill in the art was dispositive: "There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." *Id.* Since the level of skill in the present art is high, such practitioners are aptly suited to make and use the claimed compositions in accordance with the guidance of the present disclosure.

When balancing the *In re Wands* factors, it is apparent in view of the foregoing remarks that the specification enables the cited claims and an indication to that effect is respectfully requested at this time.

Written Description:

The Examiner asserts at page 2 of the Office Action that claims 12-13 contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the

claimed invention. In fact, this is the only assertion made by the Examiner that pertains directly to the written description requirement. All other comments made by the Examiner in paragraph 2 of the Office Action relate to the enablement requirement.

At the outset, Applicants believe that the Examiner has not satisfied the burden of establishing that the specification does not satisfy the written description requirement, which it does. On the contrary, the Examiner's rejection merely states with unsubstantiated generality that the specification does not satisfy the written description requirement. The Examiner is respectfully reminded that comments made in the Office Action concerning the enablement rejection are not necessarily applicable to the written description rejection because the written description requirement is a separate requirement for patentability from the enablement requirement. *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 920-921 (Fed. Cir. 2004) ("We agree with Pfizer that our precedent recognizes a [separate] written description requirement. . ."). As such, Applicants believe that the Examiner has not adequately satisfied the burden of establishing that the written description rejection is not supposedly met pursuant to MPEP § 2163.04. Absent a specific rejection having a sound legal basis on this issue, the written description requirement is deemed satisfied.

III. Claim 1 Is Definite

Claim 1 stands rejected under 35 U.S.C. § 112, ¶2. In particular, the Examiner asserts at page 3 of the Office Action that the scope of claim 1 is unclear because claim 1 requires at least one of R^2-R^5 being (C_1-C_6)alkyl and in compounds 1-4 and 9-10 of claim 11, R^2-R^5 are all hydrogen. Applicants respectfully traverse the rejection.

Claim 1 defines in part a compound of formula I wherein R^2, R^3, R^4 and R^5 are each independently hydrogen or (C_1-C_6)alkyl optionally substituted with 1 to 3 halo groups with the proviso that at least one of R^2, R^3, R^4, and R^5 is (C_1-C_6)alkyl. That is, each of R^2, R^3, R^4 and R^5 can be either (i) hydrogen; or (ii) (C_1-C_6)alkyl optionally substituted with 1 to 3 halo groups, with the proviso that at least one of R^2, R^3, R^4, and R^5 is (C_1-C_6)alkyl. Claim 1 on its face is definite because those of skill in the art given the benefit of the present disclosure would readily understand the metes and bounds of claim 1. Yet, the Examiner asserts that claim 1 is indefinite insofar as claim 11 defines a compound selected from certain species, wherein compounds 1-4 and 9-10 each define R^2, R^3, R^4, and R^5 as being hydrogen.

At the outset, Applicants respectfully question the indefiniteness rejection of claim 1 since the Examiner appears to be basing the rejection on the subject matter of claim 11. As mentioned above, claim 11 is currently amended to be an independent claim. Consequently, claim 11 as amended does not depend from claim 1, and thus does not incorporate each and every feature of claim 1. While not expressly rejected by the Examiner, claim 11 is definite at least because those of skill in the art given the benefit of the present disclosure, notably at page 6, line 33-page 7, line 18, would readily be able to ascertain the metes and bounds of claim 11. As such, it is now irrelevant that compounds 1-4 and 9-11 of claim 11 define R^2, R^3, R^4 and R^5 as being hydrogen.

In view of the foregoing remarks, removal of the present rejection is respectfully requested at this time.

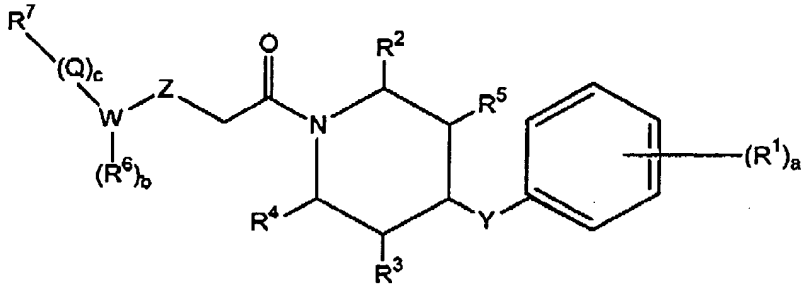
IV. Claims 1-2, 4-9, and 12-13 Are Patentable Over Domany

Claims 1-2, 4-9, and 12-13 stand rejected under § 102(g) over Domany. Applicants respectfully traverse the rejection.

The Examiner is currently rejecting claim 8, however, claim 8 is currently withdrawn pursuant to Applicant's previous election made in the "Response to Restriction Requirement" dated September 2, 2004. Thus, the present rejection with regard to claim 8 is improper and its removal is warranted.

Applicants contend that the present rejection under § 102(g) is improper. At the outset, the Examiner has not indicated which subsection of § 102(g) is relevant here to the extent that any subsection of § 102(g) is relevant, which is it not. First, Applicants contend that § 102(g)(1) is not relevant because it requires the existence of an interference under 35 U.S.C. §§ 135 or 291. As the Examiner knows, no such interference has been declared. Second, Applicants contend that § 102(g)(2) is not relevant because the Examiner has not indicated how Domany invented certain of the compounds defined by claim 1 *in the United States* before Applicants, given that the present application claims priority to a provisional application dated July 18, 2002 and Domany has a constructive reduction to practice in the United States by virtue of US national stage entry on July 21, 2004. As such, the cited claims are patentable for at least these independent, patentably significant reasons.

Nevertheless, claim 1 is patentable over Domany at least because Domany does not disclose, either explicitly or inherently, each and every feature of claim 1. Claim 1 defines in part a compound of the formula



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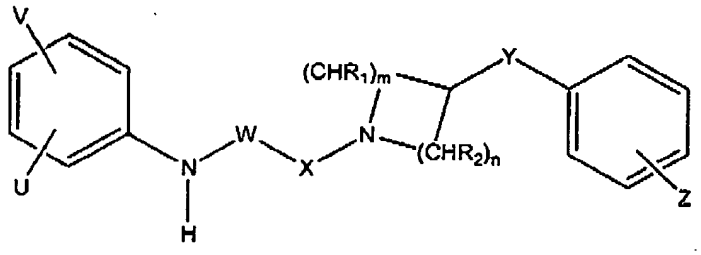
or pharmaceutically acceptable salts, tautomers, and pro-drugs thereof; wherein Z is oxygen or NR^9, where R^9 is $(C_1\text{-}C_6)$alkyl, or acetyl. Domany, on the other hand, discloses a compound of the formula



It is apparent that the compounds defined by claim 1 are novel over those disclosed by Domany at least because Domany only discloses, explicitly or inherently, compounds having a -NH group alpha to the left-hand side phenyl ring whereas the corresponding position of the compounds defined by claim 1, Z, is defined as being oxygen or NR^9, where R^9 is $(C_1\text{-}C_6)$alkyl, or acetyl. Indeed, with regard to the present compounds where Z is oxygen, the Examiner admits at page 4 of the Office Action that compounds where Z is oxygen are neither anticipated nor rendered obvious by the documents of record. As such, Domany does not disclose compounds corresponding to Applicants' Z being oxygen or NR^9, where R^9 is $(C_1\text{-}C_6)$alkyl, or acetyl. Thus, claim 1 is novel over Domany.

Claims 2, 4-7 and 9 are novel at least by virtue of their direct or indirect dependency from

claim 1. Claims 12 and 13 are novel at least by virtue of each claim defining a compound according to novel claim 1. In view of the foregoing remarks, removal of the present rejection is respectfully requested at this time.

V. Conclusion

Having addressed all outstanding issues, Applicants kindly request removal of all rejections and allowance of all pending claims at this time. To the extent the Examiner believes that it would facilitate allowance of this case, the Examiner is urged to call the undersigned at the number below.

Applicants believe that no fee is associated with the filing of this paper. However, to the extent a fee is due, the Commissioner is hereby authorized by this paper to charge any required fees or credit any overpayment to Deposit Account 16-1445.

Respectfully submitted,

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